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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---------------------------------------------------------------------------------------------------------------|-------------|----------------------|---------------------|------------------|
| 09/970,453 | 10/02/2001 | Shulamit Eyal | 20174C-002410US | 9637 |
| 20350 | 7590 | 04/26/2004 | EXAMINER | |
| TOWNSEND AND TOWNSEND AND CREW, LLP TWO EMBARCADERO CENTER EIGHTH FLOOR SAN FRANCISCO, CA 94111-3834 | | | COOK, LISA V | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1641 | |

DATE MAILED: 04/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary

Application No.

09/970,453

Applicant(s)

EYAL ET AL.

Examiner

Lisa V. Cook

Art Unit

1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 December 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☒ Claim(s) 13 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03 October 2000 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>1/31/02</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicants' Response to the Restriction Requirement mailed October 2, 2003 is acknowledged. In response to Amendment-A filed therein claims 14-18 have been canceled at Applicants request.
2. Applicant's election of Group I claims 1-13 in Fax Paper No.12/30/03 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The Restriction Requirement is deemed proper and is therefore made **FINAL**.
3. Currently, claims 1-13 are pending and under consideration.

Information Disclosure Statement

4. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or Applicant on PTO-1449 has cited the references they have not been considered.
5. The information disclosure statement filed 1/31/02 has been considered as to the merits prior to first action.

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Oath/Declaration

6. A new oath or declaration is required because provisional application number 60/237,937 filed 10/3/00 is not included and the corrected citizenship for inventor Eyal is not initialed and dated. The wording of an oath or declaration cannot be amended. If the wording is not correct or if all of the required affirmations have not been made or if it has not been properly subscribed to, a new oath or declaration is required. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

Drawings

7. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference sign(s) not mentioned in the description: Figure 7 does not identify the 1 symbol – Figure 8 does not identify the symbol j. A proposed drawing correction, corrected drawings, or amendment to the specification to add the reference sign(s) in the description, are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Specification

8. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. For example “independent” is misspelled on page 16 line 12.

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9. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See page 9 line 1. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

10. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

- (a) TITLE OF THE INVENTION.
- (b) CROSS-REFERENCE TO RELATED APPLICATIONS.
- (c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
- (d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) or
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)
- (e) BACKGROUND OF THE INVENTION.
 - (1) Field of the Invention.
 - (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
- (f) BRIEF SUMMARY OF THE INVENTION.
- (g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
- (h) DETAILED DESCRIPTION OF THE INVENTION.
- (i) CLAIM OR CLAIMS (commencing on a separate sheet).
- (j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
- (k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

11. In the instant disclosure the cross-reference (b) follows the statement regarding federally sponsored research (c).

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12. The use of several trademarks is noted in this application. They should be capitalized wherever they appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks. (For example, see pages 22,–YOYO-1).

Claim Objections

13. Claim 13 is objected to because of the following informalities: In claim 13 the word “an” appears to be missing. Step (A) line 5-6 read “parameter is [an] integrated peak are”. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 1 is vague and indefinite because it is not clear as to what is being measured. Is the method detecting a “velocity independent characteristic parameter of an analyte” or “the characteristic parameter of the analyte (which is influence or dependent on velocity)”. It is not clear if Applicant intends to use the wording interchangeably to measure the same characteristic.

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If applicant intends to recite that “the characteristic parameter” will be normalized to eliminate velocity dependency, this should be clearly set forth. Presently the claims read on the elimination of a “velocity component” in step (c), however no velocity component appears to have been measured or detected. Please correct appropriately.

B. Claim 2, is indefinite because a “velocity independent flow cytometry” is not defined by the claims or the disclosure. Accordingly the metes and bounds of the claims cannot be determined. If applicant intends to claim a flow cytometer that comprises specific configurations that negates a velocity measure, the particulars should be recited. However Applicant is cautioned as to not add new matter. If applicant merely means that the method will include conventional flow cytometry, then the “velocity independent” language should be removed from the claim in order to obviate this rejection.

C. The term “the substantially” in claim 5 is a relative term which renders the claim indefinite. The term “substantially” is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear if all the analytes are detected or not?

D. Claim 5 recites the limitation “each detection zone” in claim 3. There is insufficient antecedent basis for this limitation in the claim. Appropriate correction is required.

E. Claim 6 is indefinite because it is recited in improper Markush format. It is not clear if the detector includes all of the listed parameters or only one. Please clarify.

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F. Claim 8 is vague and indefinite because it is not clear as to how the measure time differences will be employed to eliminate velocity when velocity or factors dependent on velocity are not recited or eliminated from the claimed method. Please expound or correct claim language appropriately.

G. Claim 9 recites the limitation "first and second detection zones" in claim 8. There is insufficient antecedent basis for this limitation in the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

I. Claims 1-5 and 8-9 are rejected under 35 U.S.C. 102(e) as being anticipated by Kopf-Sill et al. (US Patent #6,613,512) or Kopf et al. (US Patent #6,524,790).

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Kopf-Sill et al. disclose methods and microfluidic devices to measure reactants and reaction products while considering velocity. See column 1 line 64 through column 2 line 23. Reactants and products with different velocities (characteristics of an analyte) are measured in a microfluidic channel. See column 2 lines 36-37 and lines 57-58. In one embodiment the fluid samples are transported from a first position to a second position by electroosmotic flow (claim 4). See column 6 lines 15-18. The time dependent data generated is processed to include baseline subtraction and masking for accurate measurements of the analyte of interest (normalizing and considering velocity). See column 1 lines 64-67 and column 22 lines 18-42.

Multiple detection positions/zones are taught at two different time points in figure 1. See figure 1 Time= t_2 and Time $>t_2$ (time difference measurement). The time difference and velocity are utilized in an equation to accurately measure the characteristic of interest in the analyte (claims 8 and 9). See column 5 line 11 through column 6 line 43. The various reactants and products can be assessed serially (individually) or simultaneously in the methods (claim 5). See column 2 lines 34-35.

Kopf-Sill et al. teach the step of normalizing or eliminating the velocity component in reaction measurements. See column 5 lines 55-62 and column 8 lines 10-22.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

II. Claims 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kopf-Sill et al. (US Patent #6,613,512) or Kopf-Sill et al. (US Patent #6,524,790) in view of Squire et al. (Journal of Microscopy, 197(2) 2/2000, 136-149).

Please see Kopf-Sill et al. (US Patent #6,613,512) or Kopf-Sill et al. (US Patent #6,524,790) as set forth above.

Kopf-Sill et al. (US Patent #6,613,512) or Kopf et al.-Sill (US Patent #6,524,790) differ from the instant invention in failing to teach acousto-optic modulators.

However, Squire et al. teach methods for measuring fluorescence with wave acoustic-optic modulators placed in a series. This configuration analyzed multiple data sets simultaneously and distinctly. See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use acoustic-optic modulators as taught by Squire et al. in either method of Kopf-Sill et al. (6,613,512 or 6,524,790) because Squire et al. taught that "standing wave acoustic-optic modulators provide a means of modulating a continuous wave laser in a sinusoidal manner at high frequencies. A number of these [lasers] can be employed in series to simultaneously modulate the excitation light of individual frequencies, their differences, and sums." See page 139 figure 2 and 2nd column last paragraph.

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One of ordinary skill in the art would have been motivated to utilize these lasers in order to detect multiple frequencies simultaneously. Therein evaluating several analytes.

III. Claims 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kopf-Sill et al. (US Patent #6,613,512) or Kopf-Sill et al. (US Patent #6,524,790) in view of Armstrong et al. (Cytometry, 40:102-108, 2/2000).

Please see Kopf-Sill et al. (US Patent #6,613,512) or Kopf-Sill et al. (US Patent #6,524,790) as set forth above.

Kopf-Sill et al. (US Patent #6,613,512) or Kopf et al.-Sill (US Patent #6,524,790) differ from the instant invention in failing to teach oligonucleotide detection including nucleotide measurements.

However, Armstrong et al. teach this limitation. Their methods evaluate PCR probes that are linked to fluorescent molecules and measured by flow cytometry. See abstract. The method detects individual nucleotides from individual nucleotide fluorescence peaks. See figures 2, 3, and 4.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use detect oligonucleotides and the nucleotides which make up the oligonucleotides as taught by Armstrong et al. in either method of Kopf-Sill et al. (6,613,512 or 6,524,790) because Armstrong et al. taught that genetic diversity is exhibited in disease and drug response and they can be effected by a single nucleotide difference/change/variant. See abstract.

17. For reasons aforementioned, no claims are allowed.


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18. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 872-9306, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to Group TC 1600 whose telephone number is (571) 272-1600.


Lisa V. Cook
Patent Examiner
Art Unit: 1641
Remsen 3C-59
(571) 272-0816


LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
04/19/02